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Quest to identify geochemical risk factors associated with chronic kidney disease of unknown etiology (CKDu) in an endemic region of Sri Lanka-a multimedia laboratory analysis of biological, food, and environmental samples. < <https://doi.org/10.1007/s10661-016-5524-8>>

Levine, K. E., Redmon, J. H., Elledge, M. F., Wanigasuriya, K. P., Smith, K., Munoz, B., ... Wickremasinghe, R. (2016).

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The emergence of a new form of chronic kidney disease of unknown etiology (CKDu) in Sri Lanka's North Central Province (NCP) has become a catastrophic health crisis. CKDu is characterized as slowly progressing, irreversible, and asymptomatic until late stages and, importantly, not attributed to diabetes, hypertension, or other known risk factors. It is postulated that the etiology of CKDu is multifactorial, involving genetic predisposition, nutritional and dehydration status, exposure to one or more environmental nephrotoxins, and lifestyle factors. The objective of this limited geochemical laboratory analysis was to determine the concentration of a suite of heavy metals and trace element nutrients in biological samples (human whole blood and hair) and environmental samples (drinking water, rice, soil, and freshwater fish) collected from two towns within the endemic NCP region in 2012 and 2013. This broad panel, metallomics/mineralomics approach was used to shed light on potential geochemical risk factors associated with CKDu. Based on prior literature documentation of potential nephrotoxins that may play a role in the genesis and progression of CKDu, heavy metals and fluoride were selected for analysis. The geochemical concentrations in biological and environmental media areas were quantified. Basic statistical measurements were subsequently used to compare media against applicable benchmark values, such as US soil screening levels. Cadmium, lead, and mercury were detected at concentrations exceeding US reference values in many of the biological samples, suggesting that study participants are subjected to chronic, lowlevel exposure to these elements. Within the limited number of environmental media samples, arsenic was determined to exceed initial risk screening and background concentration values in soil, while data collected from drinking water samples reflected the unique hydrogeochemistry of the region, including the prevalence of hard or very hard water, and fluoride, iron, manganese, sodium, and lead exceeding applicable drinking water standards in some instances. Current literature suggests that the etiology of CKDu is likely multifactorial, with no single biological or hydrogeochemical parameter directly related to disease genesis and progression. This preliminary screening identified that specific constituents may be present above levels of concern, but does not compare results against specific kidney toxicity values or cumulative risk related to a multifactorial disease process. The data collected from this limited investigation are intended to be used in the subsequent study design of a comprehensive and multifactorial etiological study of CKDu risk factors that includes sample collection, individual surveys, and laboratory analyses to more fully evaluate the potential environmental, behavioral, genetic, and lifestyle risk factors associated with CKDu.

Deciphering chronic kidney disease of unknown etiology in Sri Lanka. In Improving Outcomes for Noncommunicable Diseases in Low- and Middle-Income Countries

<<https://doi.org/10.3768/rtipress.2016.bk.0017.1608>>

Redmon, J., Elledge, M., Wanigasariya, KP., Wickremasinghe, RJ., & Levine, K. (2016). (pp. 105-126). North Carolina: RTI Press

Noncommunicable diseases (NCDs) are the main cause of death worldwide. The incidence, prevalence, and death rates from NCDs are expected to increase in the future. No single discipline can address the issues of prevention, early detection, access to care, and appropriate treatment that are needed to improve outcomes for NCDs; this will require transdisciplinary collaborations. Given the tremendous impact of NCDs on morbidity, mortality, and costs worldwide, there is little doubt that efforts to improve NCD outcomes are worthwhile.

The projects described in this book focus on the risk factors for treatment of the NCDs responsible for the greatest impact on morbidity and mortality: cardiovascular disease, cancer, diabetes, and chronic respiratory diseases. The pilot projects were carried out in low- and middle-income countries, which are disproportionately affected by NCDs. The lessons learned from these initial pilot projects have great potential to be increased in scale to reduce the devastating impact of noncommunicable diseases.

Additional perspectives on chronic kidney disease of unknown aetiology (CKDu) in Sri Lanka - lessons learned from the WHO CKDu population prevalence study. <<https://doi.org/10.1186/1471-2369-15-125>>

Redmon, J., Elledge, M., Womack, D., Wickremashinghe, R., Wanigasuriya, KP., Peiris-John, RJ., ... Levine, K. (2014). BMC Nephrology, 15, 125.

The recent emergence of an apparently new form of chronic kidney disease of unknown aetiology (CKDu) has become a serious public health crisis in Sri Lanka. CKDu is slowly progressive, irreversible, and asymptomatic until late stages, and is not attributable to hypertension, diabetes, or other known aetiologies. In response to the scope and severity of the emerging CKDu health crisis, the Sri Lanka Ministry of Health and the World Health Organization initiated a collaborative research project from 2009 through 2012 to investigate CKDu prevalence and aetiology. The objective of this paper is to discuss the recently published findings of this investigation and present additional considerations and recommendations that may enhance subsequent investigations designed to identify and understand CKDu risk factors in Sri Lanka or other countries.

Chronic kidney disease of unknown etiology in Sri Lanka: Quest for understanding and global implications. <<https://doi.org/10.3768/rtipress.2014.rb.0007.1405>>

Elledge, M., Redmon, J. H., Levine, K., Wickremasinghe, R.J., Wanigasariya, K.P., & Peiris-John, R.J. (2014). (RTI Press Publication No. RB-0007-1405). Research Triangle Park, NC: RTI Press.

This research brief examines chronic kidney disease of unknown etiology (CKDu) in Sri Lanka. A new and growing public health challenge that has emerged in Sri Lanka, CKDu is epidemic in selected geographic areas of the country, primarily in its central and eastern dry zones. CKDu is not attributed to diabetes, hypertension, or other factors commonly associated with chronic kidney disease. A number of risk factors point to environmental triggers for the onset of CKDu, but evidence so far is insufficient to accurately pinpoint the potential cause or causes. Small studies conducted to date attempt to associate CKDu with agrochemicals, ayurvedic (traditional) medicines, water quality, or other environmental or lifestyle factors. This complex emerging health crisis requires an interdisciplinary approach, following strict field protocols and a rigorous environmental health risk assessment framework. Research and analysis to better understand CKDu are important for Sri Lanka and have global implications for understanding of similar geographic CKDu “hot spots” in Central America, Eastern Europe, and South Asia.

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